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1645

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. <b>09/887,773</b>	Applicant(s) <b>Cowden et al.</b>
	Examiner <b>S. Devi, Ph.D.</b>	Art Unit <b>1645</b>

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)  Responsive to communication(s) filed on May 16, 2002

2a)  This action is **FINAL**.      2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

4)  Claim(s) 22-28 is/are pending in the application.

4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 22-28 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are a)  accepted or b)  objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)  The proposed drawing correction filed on \_\_\_\_\_ is: a)  approved b)  disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12)  The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)  Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some\* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

14)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a)  The translation of the foreign language provisional application has been received.

15)  Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)      4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_

2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)      5)  Notice of Informal Patent Application (PTO-152)

3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_      6)  Other: \_\_\_\_\_

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## **DETAILED ACTION**

### **Preliminary Amendment**

1) Acknowledgment is made of preliminary amendment filed 06/21/01 (paper no. 2).

### **Election**

2) Acknowledgment is made of Applicants' election filed 05/16/02 (paper no. 4) in response to the restriction requirement mailed 04/16/02 (paper no. 3). Applicants have elected invention I, claims 22-28, and have canceled the non-elected claims 9-14.

### **Status of Claims**

3) Claims 9-14 have been canceled via the amendment filed 05/16/02.  
Claims 1-8 and 15-21 have been canceled via the amendment filed 06/21/01.  
Claims 22-28 have been elected via the election filed 05/16/02.  
Claims 22-28 are pending and are under examination.

### **Priority / Continuity**

4) The instant application is a continuation of application SN 09/142,597, filed 03/05/1999, *now pending*, which is a 371 of PCT/AU97/00161, filed 03/14/1997 and claims foreign priority to application, PN 8703, filed 03/14/1996 in Australia.

### **Drawings**

5) The drawing submitted in the instant application is not objected to by the Draftsperson under 37 CFR 1.84 or 1.152 and as such, the drawing has been approved as a formal drawing. A copy of the PTO 948 is attached to this Office Action (paper no. 5).

### **Specification - Informalities**

6) The instant specification is objected to for the following reason(s):  
A) The instant application is partly informal in the format or arrangement of the specification. The following guideline illustrates the preferred layout and content for patent applications. The subheading 'Brief Summary of the Invention' is missing on page 18. The guideline is suggested for the Applicants' use.

### **Content of Specification**

(f) **Brief Summary of the Invention:** A brief summary or general statement of the

invention as set forth in 37 C.F.R 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

B) The first paragraph of the specification does not accurately reflect the current status of the prior application as indicated above under 'priority/continuity in italicized words. Correction is requested.

#### **Rejection(s) under 35 U.S.C § 101**

7) Claims 22-28 are rejected under 35 U.S.C. § 101, because the claimed invention is directed to non-statutory subject matter. Claims are drafted in terms of "use" and these are not proper process claims under 35 U.S.C. § 101. "Use" is not one of the statutory classes of invention. See *Clinical Products v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966) and *Ex Parte Dunki*, 153 USPQ 678 (Bd. App. 1967).

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#### **Rejection(s) under 35 U.S.C § 112, Second Paragraph**

8) Claims 22-28 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claims 22-28 are indefinite, because the claims merely recite a "use" without reciting any active positive steps as to how the use is actually practiced. It is suggested that Applicants use the recitation --A method of use--.

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(b) Claim 22 is vague and indefinite in the recitation "analogous or homologous" components, because it is unclear what is encompassed in this limitation. Since the parameters for determining the analogy or homology of one antigenic component relative to another are not

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defined, it is not clear what constitutes analogous or homologous components. It is unclear which characteristics an antigen should have in order to qualify as an "analogous or homologous" antigenic component.

*What degree of homo*

(c) Claims 24 and 28 are vague and confusing in the use of the abbreviation in the claim language: "IDDM" or "QFA". It is suggested that the abbreviation be recited as a full terminology at first occurrence, with its abbreviated recitation retained in parentheses.

(d) Claim 22 is confusing and/or redundant in the recitation "component components therefrom" (see lines 1 and 2), because it is unclear what is encompassed in the limitation. Claim 22 is further confusing and/or incorrect in the recitation "in the manufacture of a medicament in the treatment". Do Applicants mean that the antigenic component is used in the manufacture of a medicament "for the treatment" of the recited disease. Clarification/correction is requested.

(e) Claims 23-28, which depend directly or indirectly from claim 22, are also rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, because of the indefiniteness or vagueness identified above in the base claim(s).

#### **Rejection(s) under 35 U.S.C § 112, First Paragraph**

9) Claims 22-28 are rejected under 35 U.S.C § 112, first paragraph, because the specification, while being enabling for a method of use of a *Coxiella burnetii* QVAX vaccine or QFA antigen in the manufacture of a medicament meant for treatment of IDDM in a mammal, does not reasonably provide enablement for a method of use of any antigenic component, analogue and homologue thereof of any species of *Coxiella* other than *Coxiella burnetii* in the manufacture of a medicament for the treatment of any autoimmune disease other than IDDM or autoimmune coxiellosis.

The instant claims are evaluated based on the *Wands* analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

- The quantity of experimentation necessary (time and expense);
- The amount of direction or guidance presented;
- The presence or absence of working examples of the invention;
- The nature of the invention;

- The state of the art;
- The relative skill of those in the art;
- The predictability or unpredictability of the art; and
- The breadth of the claims.

In the instant case, the nature of the invention is related to the use of antigenic component(s) of *Coxiella burnetii*, or antigenic components “analogous or homologous” to one or more antigenic components of a species of *Coxiella*, or *Coxiella burnetii* in particular, in the manufacture of a medicament for the treatment of an autoimmune disease, IDDM in particular. Although the relative skill of those in this art is high, the breadth of the claims encompasses the use of any *Coxiella* antigen, or antigenic components analogous or homologous to one or more antigenic components of *Coxiella*, for use in the claimed method against any autoimmune disease. However, neither *Coxiella* antigens, nor antigenic components analogous or homologous to the antigenic components of a species of *Coxiella*, or *Coxiella burnetii* in particular, other than QFA or QVAX, are identified and enabled for use in the manufacture of the medicament. The only working examples are directed to QFA and QVAX, both antigenic components of *Coxiella burnetii*. Though any composition containing QFA would likely to work similarly to QFA, one skilled in the art would not expect every *Coxiella* antigen to work. No further guidance is given as to what other antigens would and would not work.

The applied art (see below) establishes that some antigens of *C. burnetii* are successfully used to treat autoimmune coxiellosis. However, with regard to the treatment of any non-coxiella-related autoimmune diseases, the specification does not teach how to identify the precise antigenic components that allegedly prevent, inhibit, delay onset of or ameliorate the effects of the broadly recited autoimmune disease, or provide any specific teachings of how to reproducibly produce these antigenic autoimmune-ameliorating antigenic components for use in a method of manufacture of a medicament.

The art, as applied below, teaches a specific mycobacterial antigenic component that is analogous or homologous to an antigenic component of *Coxiella burnetii* and demonstrates a method of use of such antigenic component in the manufacture of a medicament for the treatment of IDDM. The claims, as drafted currently, encompass a method of use of antigenic components,

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microbial or non-microbial, analogous or homologous to any species of *Coxiella*, including *Coxiella burnetii*, in the manufacture of a medicament for the treatment of any autoimmune diseases, including IDDM. However, the parameters for determining the analogousness or homologousness of one antigen relative to another antigen are not disclosed. Clearly, the full scope of the claims is not commensurate with the enabling disclosure or evidence. Without specific identification and disclosure of the production of non-*Coxiella burnetii* antigenic components that are analogous or homologous to the antigenic components of *Coxiella burnetii* and without a demonstration of, or specific guidance as to how to use such antigenic components in the claimed method, one of ordinary skill in the art would not be able to practice the full scope of the invention and therefore, would not be able to reproducibly practice the claimed invention without undue experimentation. Given the lack of disclosure and/or guidance in the specification, the breadth of the claims, quantity of experimentation required and the unpredictability associated with identifying such antigenic components, microbial or non-microbial, one of ordinary skill in the art could not practice the full scope of the claimed invention, without undue experimentation. The ability to reproducibly practice the full scope of the claimed method is well outside the realm of routine experimentation. The claims are viewed as not meeting the scope of enablement provisions of 35 U.S.C § 112, first paragraph.

#### **Rejection(s) under 35 U.S.C. § 102**

**10)** The following is a quotation of the appropriate paragraph(s) of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

**(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**11)** Claims 22, 23 and 25-28 are rejected under 35 U.S.C § 102(b) as being anticipated by Zhang *et al.* (*Acta Virologica* 38: 327-332, 1994), or Gajdosova *et al.* (*Acta Virologica* 38: 339-344, 1994), or Williams *et al.* (*Infect. Immun.* 51: 851-858, 1986) as evidenced by Levy *et al.* (*Eur. J. Epidemiol.* 5: 447-453, 1989, abstract), or Roue *et al.* (*Lancet* 341: 1094-1095, 1993).

Zhang *et al.* teach a method of making a subunit vaccine composition comprising a purified antigenic outer membrane protein component of *Coxiella burnetii* for administration to

mice and guinea pigs, in which the composition confers protection against challenge with *Coxiella burnetii* (see abstract; page 328, left column; Table 2 and Figure 2). Zhang *et al.* also teach the use of a suspension of killed phase I whole cells of *Coxiella burnetii* (i.e., QFA) as a vaccine for use in humans and animals (see page 327, left column).

Similarly, Gajdosova *et al.* teach a method of making a composition comprising phase I *Coxiella burnetii* whole cells or Cb I (i.e., QFA) and/or outer membrane components of *Coxiella burnetii* by combining with a pharmaceutically acceptable carrier for administration to mice (i.e., mammal or a laboratory test animal) for induction of protective humoral and cellular immunity (see abstract; 'Materials and Methods'; and 'Discussion'). A method of preparing a Cb I and an OMC, i.e., a phase I trichloracetic extract (i.e., an antigenic component of *C. burnetii*) for immunization of mice which conferred highest degree of protection or resistance against challenge with *Coxiella burnetii* is taught (see abstract and page 343, left column, second full paragraph).

Williams *et al.* disclose a method of making a vaccine comprising phase I *Coxiella burnetii* chloroform-methanol residue (CMRV) or whole cell vaccine (WCV) which induced active immunity or protection against Q fever in 80% and 50% of mice (i.e., mammals or laboratory test animals) respectively. See abstract; and page 852, left column.

That the prior art methods involve the use of one or more antigenic components of *Coxiella burnetii* in the manufacture of a therapeutic composition or medicament for the treatment of an autoimmune disease in a mammal is inherent from the teachings of Zhang *et al.* or Gajdosova *et al.* in light of what is known in the art. For instance, Levy *et al.* teach the association between Q fever and autoimmune disorder by providing serological evidence of existence or development of autoimmune antibodies (see abstract), and Roue *et al.* teach that acute Q fever is associated with autoimmune disorders and development of autoimmune serological markers (see entire document, especially last paragraph).

The disclosure of Zhang *et al.* or Gajdosova *et al.* or Williams *et al.* anticipates the instant claims. Levy *et al.* or Roue *et al.* is **not** used as a secondary reference in combination with Zhang *et al.* or Gajdosova *et al.* or Williams *et al.*, but rather is used to show that every element of the

claimed subject matter is disclosed by Zhang *et al.* or Gajdosova *et al.* or Williams *et al.* See *In re Samour* 197 USPQ 1 (CCPA 1978).

12) Claims 22-28 are rejected under 35 U.S.C. § 102(b) as being anticipated by Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) as evidenced by Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988) and Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995).

Qin *et al.* teach a method of producing a therapeutic composition (i.e., medicament) by combining an emulsion of CFA or complete Freund's adjuvant with saline, i.e., a pharmaceutically acceptable carrier or diluent, for treating the development of type I diabetes (i.e., IDDM) in non-obese diabetic (NOD) mice, i.e., laboratory mammalian test animals. CFA contains the adjuvanting cell wall of *Mycobacterium* strain, H37Ra (i.e., *M. tuberculosis*). See abstract; paragraph bridging pages 2072 and 2073; and second paragraph under 'Materials and Methods'. Qin *et al.* also teach that CFA treatment prevents the adverse effects, or the autoimmune destruction of transplanted syngeneic islets in diabetic NOD mice (see page 2073, left column, lines 4-6).

That the prior art antigenic component contained in CFA necessarily serves as an antigen "analogous or homologous" to an antigenic component of *C. burnetii* is inherent from the teachings of Qin *et al.* in light of what is known in the art. For instance, Vodkin *et al.* teach that the immunogenic heat shock protein (HSP) antigen (i.e., the antigenic component) of *Coxiella burnetii* is "homologous" to a hsp (heat shock protein) polypeptide of mycobacterial species, including *M. tuberculosis*, and has potential as an efficacious vaccine (see abstract, and the third full paragraph in the left column on page 1230). Edginton teaches that Freund's complete adjuvant (i.e., CFA) contains a mixture of highly conserved mycobacterial hsp (see page 1443, left column, first full paragraph). Edginton discloses that hsp serve as natural stand-alone adjuvants (see page 1443, last paragraph).

The disclosure of Qin *et al.* anticipates the instant claims. Vodkin *et al.* or Edginton is not used as a secondary reference in combination with Qin *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Qin *et al.* See *In re Samour* 197 USPQ 1 (CCPA 1978).

**Rejection(s) under 35 U.S.C. § 103**

13) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

14) Claims 22-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Qin *et al.* (*J. Immunol.* 150: 2072-2080, 1993) in view of Vodkin *et al.* (*J. Bacteriol.* 170: 1227-1234, 1988), Edgington (*Biotechnology* 13: 1442-1444, 13 December 1995) and Barnes *et al.* (WO 87/06590).

Qin *et al.* teach a method of producing a therapeutic composition (i.e., medicament) by combining an emulsion of CFA or complete Freund's adjuvant with saline, i.e., a pharmaceutically acceptable carrier or diluent, for treating against the development of type I diabetes (i.e., IDDM) in non-obese diabetic (NOD) mice, i.e., mammalian laboratory test animals. CFA contains the adjuvanting cell wall of *Mycobacterium* strain, H37Ra (i.e., *M. tuberculosis*). See abstract; paragraph bridging pages 2072 and 2073; and second paragraph under 'Materials and Methods'. Qin *et al.* also teach that CFA treatment prevents the adverse effects, or the autoimmune destruction of transplanted syngeneic islets in diabetic NOD mice (see page 2073, left column, lines 4-6). Qin *et al.* do not expressly teach that the antigenic component contained in CFA is "analogous or homologous" to an antigenic component of *C. burnetii*.

However, Vodkin *et al.* teach that the immunogenic heat shock protein (HSP) antigen (i.e.,

the antigenic component) of *Coxiella burnetii* is “homologous” to a hsp (heat shock protein) polypeptide of mycobacterial species, including *M. tuberculosis*, and has potential as an efficacious vaccine (see abstract, and the third full paragraph in the left column on page 1230). The protein is immunogenic in mice, elicits antibodies against *Coxiella burnetii* and is suggested as a subunit vaccine against Q fever (see the last paragraph under ‘Discussion’). Vodkin *et al.* also disclose a whole cell lysate (i.e., QFA) of *C. burnetii* that contains the homologous antigenic component (see page 1230, second full paragraph, and Figure 7).

Edgington teaches that Freund’s complete adjuvant (i.e., CFA) contains a mixture of highly conserved mycobacterial hsps (see page 1443, left column, first full paragraph). Edginton discloses that hsps serve as natural stand-alone adjuvants (see page 1443, last paragraph). Edginton also teaches that the “general opinion that links hsps to diabetes ... is simply uninformed” (see abstract, and page 1443, left column, first full paragraph).

Barnes *et al.* disclose the disadvantages of using Freund’s complete adjuvant for *in vivo* use. Barnes *et al.* teach that when used with an antigen in an injectable form, large lesions often form at the site of injection, which render the adjuvant unsatisfactory for use in humans, pets and in meat animals (see page 1, fourth full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace Qin’s CFA with Vodkin’s immunogenic *Coxiella burnetii* HSP antigenic component in Qin’s method, or the *Coxiella burnetii* whole cell preparation or lysate, to produce the method of the instant invention, with a reasonable expectation of success, because CFA is known in the art to contain highly conserved mycobacterial hsps as taught by Edginton, and mycobacterial hsps are known in the art to be homologous to the *Coxiella burnetii* antigenic HSP component as taught by Vodkin *et al.* Given the art-recognized adjuvanting function of highly conserved bacterial hsps and the knowledge that these hsps are not linked to the pathogenesis of diabetes as taught by Edginton, one skilled in the art would be motivated to produce the instant invention for the expected benefit of avoiding the art-recognized undesired large lesions associated with Qin’s CFA. Further, the substitution of one immunogenic hsp antigenic component with another, homologous, functionally equivalent, conserved, antigenic hsp

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component in a prior art method would have been obvious to a skilled artisan and would have been expected to bring about similar beneficial results or effects.

Claims 22-28 are *prima facie* obvious over the prior art of record.

#### Remarks

- 15) Claims 22-28 stand rejected.
- 16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.
- 17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June, 2002

  
S. DEVI, PH.D.  
PRIMARY EXAMINER